Factors of interest	Human and LPAI, including LPAI viruses that cause mild infections in humans	HPAI and HPAI viruses that have infected humans	Non-contemporary human viruses (e.g., H2N2)	1918 influenza virus **
Pathogenicity	+ to ++	++++	++ to ++++	unknown
Route of transmission	Large droplet and airborne	Large droplet and airborne	Large droplet and airborne	Large droplet and airborne
Agent stability	+ to ++	++	+	+
Infectious dose	1 to 10	unknown	1 to 10	1 to 10
Concentration	$10^2 \text{ to } 10^8$	$10^2 \text{ to } 10^8$	$10^2 \text{ to } 10^8$	$10^2 \text{ to } 10^{10}$
Origin	Epidemic or sporadic	Sporadic or Outbreak associated	Outbreak associated/Laboratory acquired	Laboratory acquired
Geographic source	LPAI are permit driven	Any	Laboratory	Laboratory
Data from animal studies (Virulence)	+ to ++	+ to ++++	+ to ++	Unknown***
Availability of effective prophylaxis or therapeutic intervention	Vaccines and/or antivirals	Antivirals	Antivirals	Antivirals
Medical surveillance	Recommended for LPAI	Required	Strongly recommended	Strongly recommended
Experience and skill of at-risk personnel		Specialized training	Specialized training	Specialized training

<sup>\*\*</sup> Risk assessment should be reviewed when additional data are available.

Note: Work with avian influenza viruses (LPAI and HPAI) is regulated by a permitdriven process administered by the USDA.

<sup>\*\*\*</sup> Individual genes and gene constellations are being evaluated for virulence.

## Other Factors to be considered:

- Gene constellation used
- Clonal purity
- Phenotypic stability
- Number of years since a virus that was antigenically related to the donor of the hemagglutinin and neuraminidase genes last circulated
- Clear evidence of reduced virus replication in the respiratory tract of appropriate animal models compared with the replication of wild-type parent virus from which it was derived.